Phase 3 Randomized Study of DS-1062a Versus Docetaxel in Previously Treated Advanced or Metastatic Non-Small Cell Lung Cancer With or Without Actionable Genomic Alterations

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This study has been transitioned to CTIS with ID 2023-509865-19-00 check the CTIS register for the current data. To compare the efficacy of DS-1062a with that of docetaxel, as measured by PFS and OS, for subjects with NSCLC with or without...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52040

Source
ToetsingOnline

Brief title
TROPION-LUNG01

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
Non-Small cell Lung Cancer, NSCLC

Research involving
Human

Sponsors and support

Primary sponsor: Daiichi Pharmaceutical
Source(s) of monetary or material Support: Industry

Intervention

Keyword: DS-1062a, Lung Cancer, Phase 3

Outcome measures

Primary outcome

PFS assessed by BIRC: defined as the time from randomization to the earlier of

the dates of the first radiographic disease progression or death due to any

cause.

OS: defined as the time from randomization to death due to any cause.

Secondary outcome

- PFS assessed by the investigator

- ORR

- DoR

- TTR

- DCR

- EORTC-QLQLC13 (except questions 36 and 37)

- TEAEs and other safety parameters during the study

- PK

- Immunogenicity

Study description

Background summary

Lung cancer is the most common cancer and the leading cause of cancer-related mortality worldwide, with an estimated 2.1 million new cases of lung cancer in 2018 (11.6% of all new cases) and 1.8 million deaths (18.4% of all cancer deaths) globally based on GLOBOCAN data. Advances in early detection of lung cancer have been slow, and more than half of lung cancers are still diagnosed at an advanced stage. Only 18.6% of all patients with lung cancer are alive 5 years or more after diagnosis. Non-small cell lung cancer (NSCLC) accounts for 80% to 85% of all lung cancers.

The introduction of targeted therapies and checkpoint inhibitors in recent years has improved the treatment landscape and patients with metastatic NSCLC are now surviving longer. A number of genomic alterations that have an impact on therapy selection have been identified in NSCLC and molecular testing is part of the standard of care in the evaluation of NSCLC. These include epidermal growth factor receptor (EGFR) gene mutations, anaplastic lymphoma kinase (ALK) gene rearrangements, ROS proto-oncogene 1 (ROS1) rearrangements, neurotrophic tyrosine receptor kinase (NTRK) gene fusions, and proto oncogene B-raf (BRAF) point mutations.

The expression of programmed cell death ligand 1 (PD-L1) is often assessed to select patients for immune checkpoint inhibitors. For patients with metastatic NSCLC, negative test results for EGFR and ALK, and PD-L1 levels of 50% or more (approximately 27% of patients), the National Comprehensive Cancer Network (NCCN) guidelines recommend the immune checkpoint inhibitor pembrolizumab monotherapy in first-line therapy. The recommended first-line option for patients with metastatic NSCLC, negative or unknown test results for EGFR and ALK, and PD-L1 expression levels of 1% to 49% (approximately 32% of patients) depends on the background histology: for patients with nonsquamous NSCLC, the standard of care is a combination regimen of pembrolizumab plus carboplatin/cisplatin plus pemetrexed based on the results from the KEYNOTE-189 study. For patients with squamous NSCLC, the standard of care is a combination regimen of pembrolizumab plus carboplatin plus paclitaxel (or nab paclitaxel) based on results from the KEYNOTE-407 study. For patients with less than 1% expression of PD-L1, first-line therapy usually includes platinum-based chemotherapy with or without immunotherapy.

Among patients relapsing or progressing after frontline platinum-containing doublet therapy, the Checkmate-017 and -057 studies demonstrated superior OS of nivolumab over docetaxel monotherapy in patients with squamous and nonsquamous NSCLC, respectively. Notably, the median progression-free survival (PFS) of the docetaxel control arms were 2.8 months and 4.2 months, respectively, and the median OS were 6.0 months and 9.4 months, respectively.

As a result of these and similar studies, patients with NSCLC generally receive platinum doublets and immune checkpoint inhibitors, either in combination or in sequence, as the first 1 or 2 lines of therapy. None of these therapies, however, are considered curative, and once patients have progressed after them,

therapeutic options are generally limited to cytotoxic agents deployed as monotherapy, and median survival times are less than 1 year. In the multicenter, double-blind, randomized Phase 3 study (REVEL) of docetaxel plus ramucirumab or placebo as second-line treatment for patients with Stage IV NSCLC after platinum-based therapy, the median OS for patients treated with ramucirumab plus docetaxel versus those treated with placebo plus docetaxel was 10.5 months versus 9.1 months, respectively, and the median PFS was 4.5 months versus 3.0 months, respectively. However, the addition of ramucirumab to docetaxel adds significant toxicities and the relevance of the results to a population that has failed prior immune checkpoint inhibitors remains unclear. As such, global usage of ramucirumab with docetaxel remains limited, despite broad regulatory approval.

Docetaxel monotherapy remains perhaps the most widely used treatment for patients whose NSCLC has progressed after platinum-based chemotherapy and immune checkpoint inhibitors, consistent with NCCN guidelines. The Checkmate 017, Checkmate 057, and REVEL studies suggest that these patients have median PFS of 3 months to 4 months and median survival of 6 months to 9 months. Therefore, there remains significant unmet need in patients with advanced or metastatic NSCLC.

Study objective

This study has been transitioned to CTIS with ID 2023-509865-19-00 check the CTIS register for the current data.

To compare the efficacy of DS-1062a with that of docetaxel, as measured by PFS and OS, for subjects with NSCLC with or without actionable genomic alterations

Study design

This is a global, multicenter, randomized, active-controlled, open-label Phase 3 study .

Intervention

Eligible subjects will be randomized in a 1:1 ratio to DS-1062a 6.0 mg/kg or the control treatment, docetaxel 75 mg/m2. Randomization will be stratified by histology (squamous versus nonsquamous), most immediate prior therapy included anti-PD-1/anti-PD-L1 immunotherapy (yes versus no) and geographical region (US/Japan/Western Europe versus rest of world [ROW]). No crossover between study treatment arms will be allowed.

Study burden and risks

The study contains a screening phase, treatment phase and a follow-up phase. Most of the visits will take about 2 to 4 hours,
some visits will take between 5 and 7 hours.

The subject will have to undergo several examinations, tests and/or procedures before, during and after his/her treatment. Please refer to the procedure table In the ICF and table 1 1 and 1.2 in section 1 of the protocol for more information.
In addition , questions are asked about the medical history, demographics and eligibilty questions
Subjects will also be tested for HIV and hepatitis. Female patients of childbearing potential will be tested for pregnancy .
Tumor specimen need to be provided (either from current samples or through a biopsy).

Enrollment is planned to occur over approximately 14 months, with treatment and follow-up (28-day Safety Follow-up and LTSFU) projected to continue for approximately 24 months after the last subject is enrolled. The study will continue until the overall EOS Is reached The anticipated total duration of the study is approximately 38 months
The primary completion date will occur when all subjects have had either a minimum of 9 months of follow up after start of study
treatment or have discontinued from the study , whichever occurs first.

Possible side effects that are already known are described in the Investigator's Brochure and the patient informed consent form.

Contacts

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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Has the ability to provide written informed consent by signing and dating the ICF prior to the start of any study-specific qualification procedures
2. Adults >=18 years
3. Has a life expectancy =3 months based on Investigator's opinion.
4. Has pathologically documented Stage IIIB, IIIC, or Stage IV NSCLC with or without actionable genomic alteration(s) (AGA) at the time of randomization (based on the American Joint Committee on Cancer, Eighth Edition) and meets the following criteria for NSCLC:
a. Subjects Without AGA:
- Subjects must have documented negative test results for EGFR and ALK genomic alterations. If test results for EGFR and ALK are not available, subjects are required to undergo testing performed locally for these genomic alterations.
- Subjects have no known genomic alterations in ROS1, NTRK, BRAF, MET exon 14 skipping, or RET.
- Subjects with known KRAS mutations (testing during screening is not mandatory), in the absence of any driver genomic alterations, are eligible and must meet the prior therapy requirements for subjects without actionable genomic alterations described below. These subjects must be stratified as NSCLC without AGA at the time of randomization.
b. Subjects With AGA:
- Subjects must have 1 or more documented actionable genomic alteration: EGFR, ALK, ROS1, NTRK, BRAF, MET exon 14 skipping, or RET.
5. Subjects must have documentation of radiographic disease progression while on or after receiving the most recent treatment regimen for advanced or metastatic NSCLC
6. Subject must meet the following prior therapy requirements:
Subjects without AGA must meet ONE of the following prior therapy requirements for advanced or metastatic NSCLC:
a. Received platinum-based chemotherapy in combination with α-PD-

1/α-PD-L1 monoclonal antibody as the only prior line of therapy
OR
b. Received platinum-based chemotherapy and α-PD-1/α-PD-L1 monoclonal antibody (in either order) sequentially as the only 2 prior lines of therapy
Subjects with AGA must meet the following prior therapy requirements for advanced or metastatic NSCLC:
a. Has been treated with 1 or 2 prior lines of applicable targeted therapy that is locally approved for the subject's genomic alteration at the time of screening; OR one or more of the agents specified in the protocol
b. Has received platinum-based chemotherapy as the only prior line of cytotoxic therapy
c. May have received up to one α-PD-1/α-PD-L1 monoclonal antibody alone or in combination with a cytotoxic agent.
7. Must undergo a pre-treatment tumor biopsy procedure
OR
If available, tumor tissue previously retrieved from a biopsy procedure performed within 2 years prior to the subject signing informed consent and that has a minimum of 10 × 4 micron sections or a tissue block equivalent of 10 × 4 micron sections may be substituted for the pre
treatment biopsy procedure during Screening. If a documented law or regulation prohibits (or does not approve) sample collection, then such samples will not be collected/submitted.
Note: Results from the TROP2 testing of the pre-treatment tumor biopsy will not be used to determine eligibility for the study.
8. Inclusion Criterion removed
9. Has measurable disease based on local imaging assessment using RECIST v1.1
10. Has an Eastern Cooperative Oncology Group performance status ECOG PS) of 0 or1 at Screening
11. Within 7 days before randomization, has adequate bone marrow function as detailed in the study protocol
12. Within 7 days before randomization, has adequate hepatic function as detailed in the study protocol
13. Within 7 days before randomization, has adequate renal function, including mild or moderate renal function, as detailed in the study protocol
14. Has left ventricular ejection fraction (LVEF) >=50% by either ECHO or MUGA scan within 28 days before randomization
15. Has adequate blood clotting function defined as international normalized ratio/prothrombin time and either partial thromboplastin or activated partial thromboplastin time <=1.5 × ULN
16. Has an adequate treatment washout period before randomization, as defined in the study protocol
For the full list of inclusion criteria, please see protocol section 5.1

Exclusion criteria

1. Has mixed small-cell lung cancer and NSCLC histology
2. Has spinal cord compression or clinically active central nervous system (CNS) metastases, defined as untreated and symptomatic, or requiring therapy with corticosteroids or anticonvulsants to control associated symptoms. Subjects with clinically inactive brain metastases may be included in the study. Please see additional details in the protocol
3. Has leptomeningeal carcinomatosis or metastasis
4. Had prior treatment with:
a. Any agent, including antibody-drug conjugate (ADC), containing a chemotherapeutic agent targeting topoisomerase I
b. TROP2-targeted therapy.
c. Docetaxel
5. Had prior treatment with platinum-based chemotherapy and prior immunotherapy for Stage II NSCLC disease (eg, in the neo-adjuvant or adjuvant setting) without subsequently meeting the prior therapy requirements for Stage III or metastatic NSCLC disease as described in Inclusion Criterion 6
6. Has NSCLC disease that is eligible for definitive local therapy alone
7. Has uncontrolled or significant cardiac disease as described in detail in the protocol
8. Has a history of (non-infectious) ILD/pneumonitis that required steroids, has current ILD/pneumonitis, or where suspected ILD/pneumonitis cannot be ruled out by imaging at Screening
9. Clinically severe pulmonary compromise resulting from intercurrent pulmonary illnesses including, but not limited to, any underlying pulmonary disorder, or any autoimmune, connective tissue or inflammatory disorders with pulmonary involvement, or prior pneumonectomy
10. Has significant third-space fluid retention (for example ascites or pleural effusion) and is not amenable for required repeated drainage
11. Clinically significant corneal disease
12. Uncontrolled infection requiring IV antibiotics, antivirals, or antifungals; suspected infections (eg, prodromal symptoms); or inabilityto rule out infections
13. Has known human immunodeficiency virus (HIV) infection that is not well controlled
14. Has an active or uncontrolled hepatitis B and/or hepatitis C infection, is positive for hepatitis B or C virus based on the evaluation of results of tests for hepatitis B (hepatitis B surface antigen [HBsAg], anti-hepatitis B surface antibody [anti-HBs], anti-hepatitis B core antibody [anti-HBc], or hepatitis B virus [HBV] DNA), and/or hepatitis C infection (as per hepatitis C virus [HCV] RNA) within 28 days of randomization. See section 5.2 of protocol for details.
15. Has a history of malignancy, other than NSCLC except a) adequately resected non-melanoma skin cancer, b) curatively treated in situ disease, or c) other solid tumors curatively treated, with no evidence of disease for >=3 years.
16. Concomitant medical condition that would increase the risk of toxicity in

the opinion of the Investigator
17. Toxicities from previous anticancer therapy, defined as toxicities (other than alopecia) not yet improved to NCI-CTCAE version 5.0 Grade <=1 or baseline
18. Has a history of severe hypersensitivity reactions to either the drug substances or inactive ingredients (including but not limited to polysorbate 80) of DS-1062a or docetaxel
19. History of severe hypersensitivity reactions to other monoclonal antibodies
20. Is pregnant or breastfeeding or planning to become pregnant

For the full list of exclusion criteria, please see protocol section 5.2.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-10-2021
Enrollment:	14
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	DS-1062a
Generic name:	DS-1062a

Ethics review

Approved WMO Date:	11-02-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	10-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-09-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-02-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-509865-19-00
EudraCT	EUCTR2020-004643-80-NL
Other	IND 136626
CCMO	NL76044.056.21